Computational study of synthetic and natural polymer additives — Antioxidant potential of BHA, TBHQ, BHT, and curcumin

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ABSTRACT

The antioxidant potential of commonly used synthetic and natural antioxidant additives, including butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA), *tert*–butylhydroquinone (TBHQ), and natural additive, curcumin have been studied and compared by calculating the bond dissociation enthalpy (BDE), ionization potential (IP), proton dissociation enthalpy (PDE), proton affinity (PA), and electron transfer enthalpy (ETE) values for each potential hydrogen donor site. The results indicate that, in each additive an O−H group has the highest antioxidant potential (lowest BDE value). The studied molecules can be ranked based on their antioxidant potential as follows: BHT > BHA ≈ TBHQ > curcumin *A* > curcumin D. By comparing with commonly used polymers, in each studied species, there is at least one X-H bond which has a lower BDE value than in the corresponding polymeric material. Thus, all studied additives are potentially applicable to protect polymeric materials. BHT is the best radical scavenger additive in case of the hydrogen atom transfer (HAT), and the sequential proton loss electron transfer (SPLET) mechanisms to donate a H atom, but in single electron transfer proton transfer (SETPT) curcumin could also be suitable.

1. Introduction

Pure polymeric materials are frequently found to have inferior properties, which would lead to their commercial failure. In the absence of additives, polypropylene (PP) and other polyolefins most probably would not be one of the most used polymers [1]. Due to its weak thermal oxidative stability, PP would decay in just a few weeks [2]. Therefore, additives play a significant role in processing and improving the properties of polymers used in many applications including automotives, design, packaging, constructions, electronics, telecommunication [3,4]. There are a wide variety of additives available, such as plasticizers, flame retardants, lubricants, stabilizers, colorants, antimicrobial agents, and antioxidants [5], each of them improves the properties of the polymeric materials in some way. Within the realm of additives, antioxidants are especially important as they can prevent the oxidative stress induced deterioration of the materials [6]. Furthermore, oxidative stress also effects living organisms along with food and

other commodities and thus, the importance of antioxidants exceeds the range of polymers [7]. Oxidative stress is a process which involves the attack of free radicals, which are characterized by having an unpaired electron in their outer shell, making them unstable and highly reactive [8]. Antioxidants are substances which are able to donate an electron to free radicals and thus, detoxify them [9]. There are two main types of antioxidants, synthetic and natural species. Several synthetic antioxidants are used in the chemical and food industry including butylated hydroxytoluene (BHT), octyl gallate (OG), butylated hydroxyanisole (BHA), propyl gallate (PG), *tert*–butylhydroquinone (TBHQ), and others [10]. From a structural point of view, many of these are phenolic compounds (Fig. 1).

Previous studies proved that polyphenols, either natural or synthetic, are interesting and promising compounds with many applications [11–13]. Polyphenols include hydroxyl groups, which enable them to scavenge free radicals, and hydrogen atom transfer has been identified as the primary mechanism for radical scavenging [14,15]. As environmental issues are more and more prevalent, the replacement of synthetic additives is inevitable with environmentally friendly (e.g. natural) compounds. Natural antioxidants can be found in a wide variety of natural products such as plant components (fruits, leaves, and flowers) [16], as well as

in cow milk and honey [17,18]. In many countries, a variety of spices and condiments, like turmeric and garlic, have been utilized to restrain and cure a lot of diseases [19]. Curcumin [1,7-bis (4–hydroxy-3-methoxyphenyl)−1,6-heptadiene-3,5–dione] (Fig. 2) is a widespread natural antioxidant and a commonly used spice with a yellow color, and it has two isomers, curcumin A (enol) and D (diketone) [20–22]. Curcumin has several functional groups which plays a critical role in its beneficial characteristics [23]. It is a phenolic compound, extracted from the dried rhizomes of turmeric (*curcuma longa*) [24], and it has been utilized in various cosmetics and drugs as well. Besides its antioxidant effect [25,26], it has good influence on various biological and cellular conditions, and thus, used as an anti-inflammatory [27,28], anticancer and antimutagenic [29], wound healing, and hypocholesterolemic agent [20].

In order to replace synthetic antioxidants with potent natural counterparts a comparison between such species is inevitable to find the most potent alternatives. Furthermore, the antioxidant potential of the species has to be described in a detailed manner. Therefore, three synthetic (BHT, BHA, and TBHQ) and a natural (curcumin) antioxidant additive will be compared by using computational tools. The results will be applied in the future to design polymeric recipes which contain only natural or a mixture of natural and synthetic antioxidant additives.

2. Computational methods

The geometries of all the molecules and the corresponding ionic and radical species were calculated by using the Gaussian 09 program package [30]. Three different density functional theory (DFT) methods have been used, the B3LYP functional [31–34] in combination with the 6–31G(d) basis set, and the M06 and M06–2X [35] in combination with the 6–311+*G*(d,p) basis set applied to optimize all the molecules in gas phase. These methods have been chosen to calculate the antioxidant potential of the studied species, because they have been successfully applied for similar systems [36–39]. Frequency calculations have also been carried out by using the previously optimized geometries.

To explore the antioxidant activity of the studied species three different free radical scavenging (RS) mechanisms have been considered: hydrogen atom transfer (HAT), single electron transfer proton transfer (SETPT), and sequential proton loss electron transfer (SPLET) [40–46] (Fig. 3).
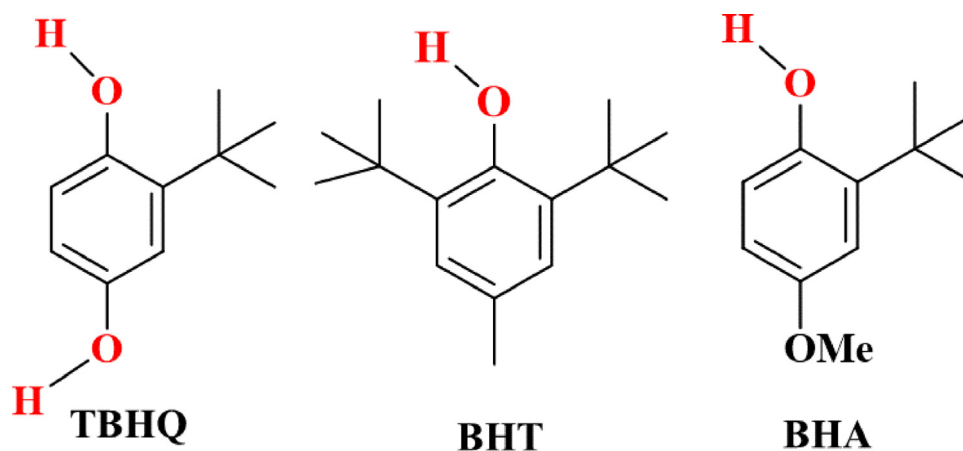

Fig. 1. Schematic representation of common synthetic antioxidants: *tert*–butylhydroquinone (TBHQ), butylated hydroxytoluene (BHT), and butylated hydroxyanisole (BHA).
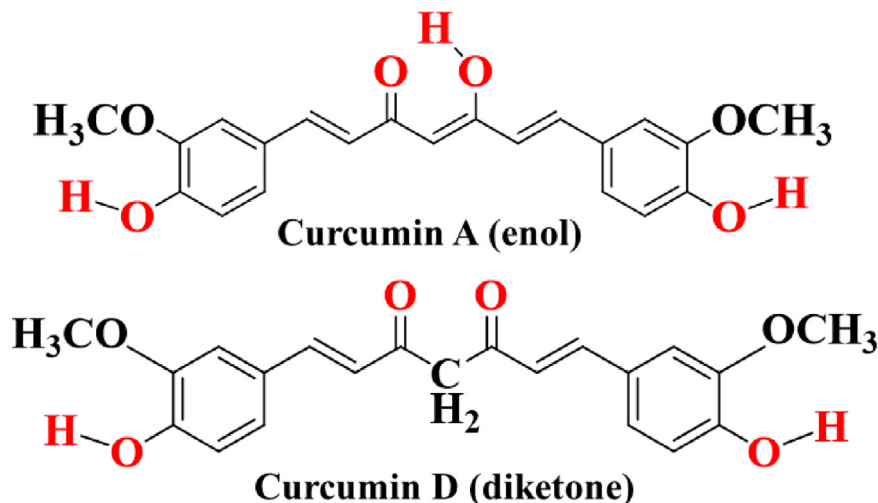

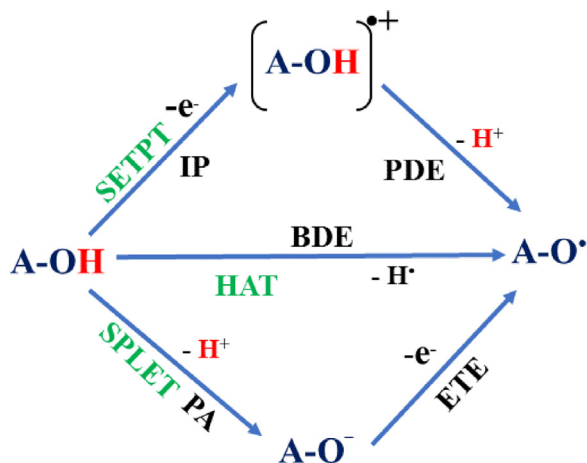**Fig. 2.** 2D chemical structure of curcumin.

Fig. 3. Radical scavenging mechanisms (hydrogen atom transfer – HAT, single electron transfer proton transfer – SETPT, and sequential proton loss electron transfer – SPLET) of phenolic antioxidants through their hydroxyl group.

To compare the antioxidant activity of the compounds, the bond dissociation enthalpy (BDE), ionization potential (IP), proton dissociation enthalpy (PDE), proton affinity (PA), and electron transfer enthalpy (ETE) has been computed for each structure as follows:

$$BDE = H(A^{.}) + H(H^{.}) - H(A) \qquad (1)$$

$$IP = H(A^{.+}) + H(e^{-}) - H(A) \qquad (2)$$

$$PDE = H(A^{.}) + H(H^{+}) - H(A^{.+}) \qquad (3)$$

$$PA = H(A^{-}) + H(H^{+}) - H(A) \qquad (4)$$

$$ETE = H(A^{.}) + H(e^{-}) - H(A^{-}) \qquad (5)$$

where $H(A)$ is the enthalpy of antioxidant, while $H(A^{.})$ and $H(H^{.})$ are the enthalpies of the corresponding antioxidant radical and hydrogen atom, respectively, which are the free radicals formed after the dissociation of an X–H (X = C, or O) bond. $H(A^{.+})$ is the enthalpy of the radical cation formed after an electron transferred from the antioxidant, while $H(A^{-})$ is the enthalpy of the anion

which is formed after a proton loss has been occurred. The corresponding values for the enthalpy of electron and proton in the gas phase were $H(e^{-}) = 3.1351$ kJ/mol and $H(H^{+}) = 6.1398$ kJ/mol, respectively [47–49].

3. Results and discussion

3.1. Validation of the selected methods

The antioxidant potential of BHA, BHT, TBHQ and curcumin (enol and diketone forms) have been studied by using three different levels of theory. Experimental O–H bond dissociation enthalpy values for BHA and BHT were used to validate the calculations and to select the best combination of method and basis set for the discussion. In each case, gas phase data were used in the comparison, and the computed values underestimated the measured BDEs (Table 1).

The least favourable choice of method would be B3LYP in combination with the 6–31G(d) basis set, as the computed BDEs are lower by >40 kJ/mol than the experimental values. By using the M06/6–311+G(d,p) level of theory, the computed BDEs improved, but the differences were still >20 kJ/mol compared to the measured values. The best method – basis set combination is the M06–2X/6–311+G(d,p) level of theory which is able to predict the BDEs with good accuracy as the difference between the calculated and experimentally measured values were only 7.5 kJ/mol and 6.0 kJ/mol for the O–H bond in BHA and BHT, respectively (Table 1). Therefore, M06–2X/6–311+G(d,p) is selected and used in the discussion to study the antioxidants. All calculations were carried out in gas phase as the validation is based on gas phase data.
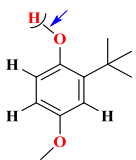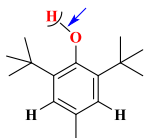
3.2. Theoretical evaluation of the antioxidant potential

3.2.1. Structural considerations

The geometries of the antioxidant additives have been optimized and it was found that the longest and shortest C–H bonds are located in BHA (C7-H) and curcumin A (C11-H), respectively (Figs. 4 and 5). As for O–H bonds, the longest one is 0.999 Å for all structures and can be found in curcumin A (O3-H). The longest bond in BHA is C7-H with a bond length equal to 1.095 Å and it is located on the methyl group in the para position, while the shortest is a benzylic hydrogen C5-H (1.081 Å). For BHT the situation is similar, and the longest C–H bond is C7-H with a bond length equal to 1.093 Å and it is located on the methyl group while

Table 1
Bond dissociation enthalpy (BDE) values (in kJ/mol) of O–H bonds in butylated hydroxytoluene (BHT), and butylated hydroxyanisole (BHA) in gas phase calculated at the B3LYP/6–31G(d), M06//6–311+G(d,p), and M06–2X/6–311+G(d,p) levels of theory.

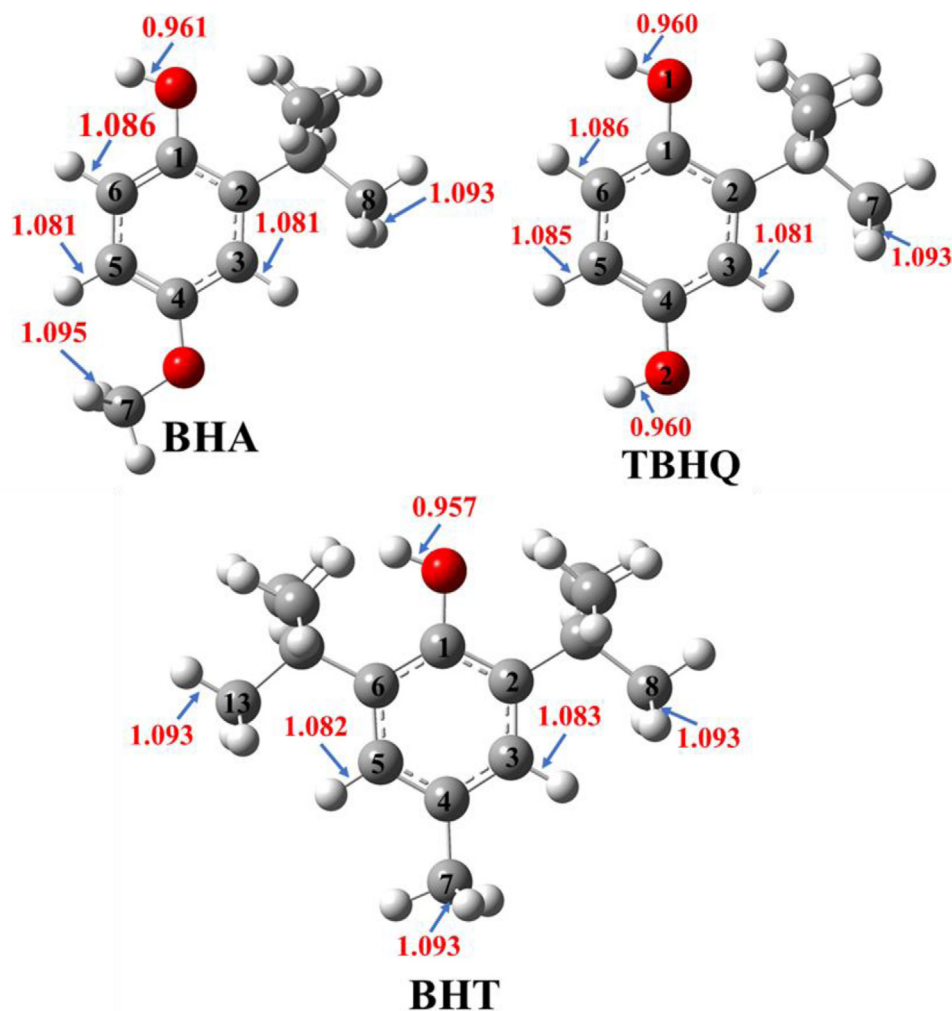| Compound	BDE(O–H) (kJ/mol)			
	B3LYP/6–31G(d)	M06/6–311+G(d,p)	M06–2X/6–311+G(d,p)	Exp. value [50]
BHA	298.0	319.3	335.9	343.4
BHT	290.3	307.9	327.0	333.0

Fig. 4. Optimized structures of the studied synthetic antioxidant additives: butylated hydroxytoluene – BHT, butylated hydroxyanisole – BHA, and *tert*–butylhydroquinone – TBHQ. The optimization have been carried out at the M06–2X/6–311+*G*(d,p) level of theory in gas phase. The corresponding bond lengths (in Å) are also shown.

the shortest bond belongs to a benzylic hydrogen C5-H (1.082 Å). In case of TBHQ, the longest C–H bond is C7-H again with a bond length equal to 1.093 Å and it is located on the methyl group, while the shortest is a benzylic hydrogen C5-H (1.085 Å) again. All in all, the bond length in each studied synthetic species follow similar trend (Fig. 4). As for the natural additive, the longest C–H bonds are located on the *o*–methoxy phenolic group on both sides of curcumin A, C1-H and C21-H, and these are equal to 1.094 Å, while the shortest bond is C11-H (1.080 Å). As for the diketone form, the longest C–H bonds are the same, C1-H and C21-H (1.094 Å), while the shortest C–H bond is located on the aromatic ring (1.083 Å).

4. Antioxidant mechanisms

In the hydrogen atom transfer (HAT) mechanism, a hydrogen atom (H·) will be directly transferred to the free radical in a one-step process. To study the effectiveness of this process, and thus, to compare the antioxidant potential of the molecules, the bond dissociation enthalpies of each unique C–H and O–H bonds in BHA, BHT, TBHQ, curcumin A, and curcumin D have been computed (Tables 2 and 3, **Fig. SI**).

The lower the BDE value, the higher the antioxidant potential as it is easier to donate the corresponding hydrogen atom to free radicals [51]. The BDEs of the O–H bonds for synthetic additives

Table 2
Bond dissociation enthalpy (BDE) values (in kJ/mol) of all unique C–H and O–H bonds in butylated hydroxytoluene - BHT, butylated hydroxyanisole - BHA, and tert–butylhydroquinone – TBHQ calculated at the M06–2X/6–311+*G*(d,p) level of theory in gas phase.

BHA	BDE	BHT	BDE	TBHQ	BDE
O-H	335. 9	O-H	327.0	O1–H	335.5
C3–H	454.4	C3-H	450.2	O2-H	345.5
C5-H	465.2	C5-H	450.1	C3-H	463.9
C6-H	464.6	C7-H	374.4	C5-H	469.3
C7-H	403.0	C8-H	417.2	C6-H	465.5
C8-H	421.3	C13-H	417.2	C7-H	420.9

are lower compared to the C–H bonds and cover a narrow range starting from 327.0 kJ/mol for BHT and reaching 345.5 kJ/mol in case of TBHQ (Fig. 6). The C–H bonds are generally stronger as the corresponding BDEs are higher than their O–H counterparts. In case of BHA, BDE$_{C-H}$ values are in a range between 403.0 and 465.2 kJ/mol. The weakest C–H bond in BHA is C7-H (1.095 Å) and it is located on the methyl group, which is in the para position, while the benzylic hydrogen C5-H (1.081 Å) is the strongest bond with a BDE = 465.2 kJ/mol (Figs. 3 and 6). The BDE values of the C–H bonds in BHT covers a range between 374.4 to 450.2 kJ/mol. C7-H (1.092 Å) has the lowest BDE$_{C-H}$ (374.4 kJ/mol) and it is lo-
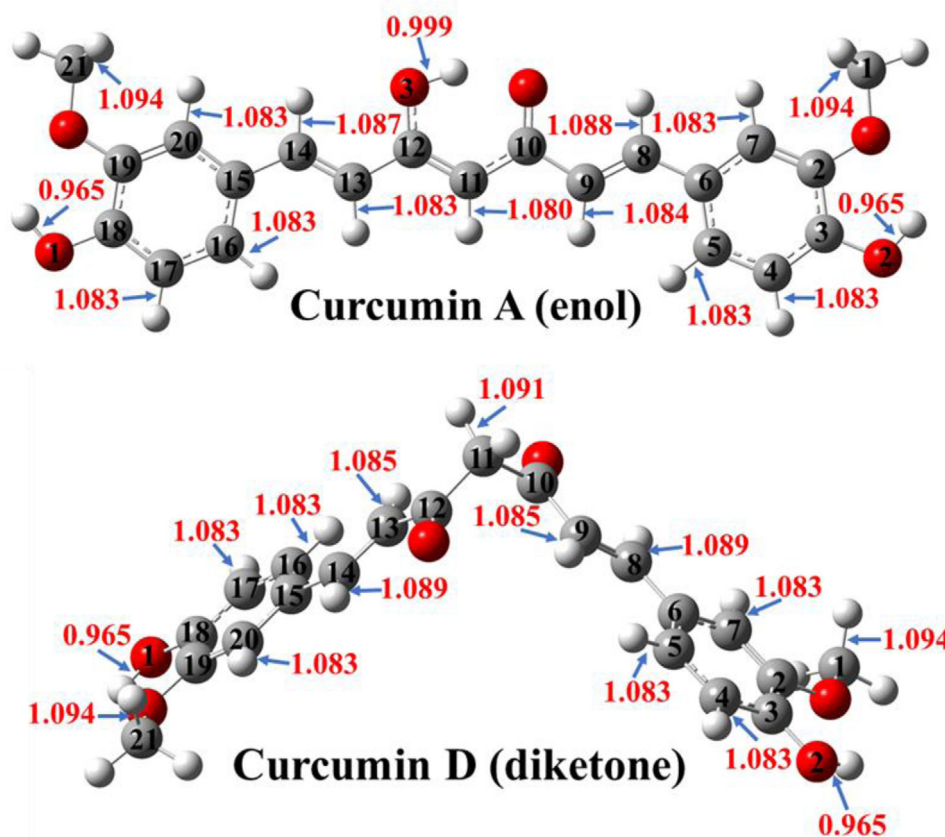
Fig. 5. Optimized geometries of the studied natural antioxidant additive structures: curcumin A and D, enol and diketone forms, respectively. The optimization have been carried out at the M06–2X/6–311+G(d,p) level of theory in gas phase. The corresponding bond lengths (in Å) are also shown.

Table 3
Bond dissociation enthalpy (BDE) values (in kJ/mol) of all unique C−H and O−H bonds in curcumin A and D calculated at the M06–2X/6–311+G(d,p) level of theory in gas phase.

Curcumin A	BDE	Curcumin D	BDE
O1-H	355.9	O1-H	359.1
O2-H	357.5	O2-H	359.1
O3-H	461.9	–	–
C1-H	408.0	C1-H	405.9
C4-H	474.5	C4-H	475.4
C5-H	464.0	C5-H	465.2
C7-H	466.8	C7-H	467.1
C8-H	438.3	C8-H	439.1
C9-H	458.8	C9-H	452.4
C11-H	482.2	C11-H	376.4
C13-H	460.2	C13-H	427.3
C14-H	439.3	C14-H	436.1
C16-H	463.4	C16-H	465.2
C17-H	474.7	C17-H	475.4
C20-H	466.6	C20-H	467.1
C21-H	407.9	C21-H	405.9

cated on the methyl group in the para position while the strongest one not surprisingly is a benzylic hydrogen, C3-H (1.083 Å) with BDE$_{C-H}$ = 450.2 kJ/mol. For TBHQ, the BDE$_{C-H}$ values cover a range between 420.9 to 469.3 kJ/mol. The smallest BDE$_{C-H}$ (420.9 kJ/mol) belongs to C7-H (1.093 Å) which is located on the methyl in the meta position, while a benzylic hydrogen (C5-H, 1.085 Å) is attached to its respective carbon via the strongest bond.

All in all, the BDE values indicate that the O−H bonds are weaker than the C−H bonds for all synthetic species and thus, the most potent functional groups within them are the hydroxyl groups (***Figure S1***). Furthermore, not surprisingly easier to remove hydrogen atoms which are part of methyl groups, than their benzylic counterparts. Based on the computed BDE values of the C−H and O−H bonds of the synthetic additives, BHT has the highest antioxidant potential. The studied natural antioxidant, curcumin has two isomers, the enol (curcumin A) and diketone (curcumin D) forms. There are three O−H bonds in curcumin A and only two in curcumin D. Four of these are very similar in terms of the computed BDE$_{O-H}$ values as these are around 355.9 and 359.1 kJ/mol. However, in the case of the enol form, O3-H has an exceptionally high BDE value (461.9 kJ/mol) as it is participating in a hydrogen bond (Figs. 5 and 6). For C−H bonds, the BDE values in case of the enol form starts from 407.9 kJ/mol and reach up to 482.2 kJ/mol. The weakest C−H bond within curcumin A is C21-H and it is located on the o−methoxy phenolic group while the strongest one is C11-H, and it has a quite high BDE value with 482.2 kJ/mol. As for the diketone form, the BDE$_{C-H}$ values cover a similar range starting from 405.9 to 475.4 kJ/mol. The weakest C−H bond in curcumin D is at the same position, C21-H whereas the strongest bond is C4-H. All in all, with one exception the O−H bonds in curcumin are weaker than the C−H bonds which follows the trend of the synthetic structures (***Fig. S1***). By comparing the computed BDE values of curcumin A and D, and the other studied species, the molecules can be ranked based on their antioxidant potential as follows: BHT > BHA ≈ TBHQ > curcumin *A* > curcumin D.

The experimental BDEs of a few commonly used polymers were collected from the literature (***Table S1***) and it was found that they are in a range of 393.7 and 406.2 kJ/mol [52]. In each studied antioxidant additive, there is at least one X-H bond which has a lower BDE than the polymers. Thus, the additives can be applied to protect the polymers and prevent the oxidative stress induced deterioration of the materials.
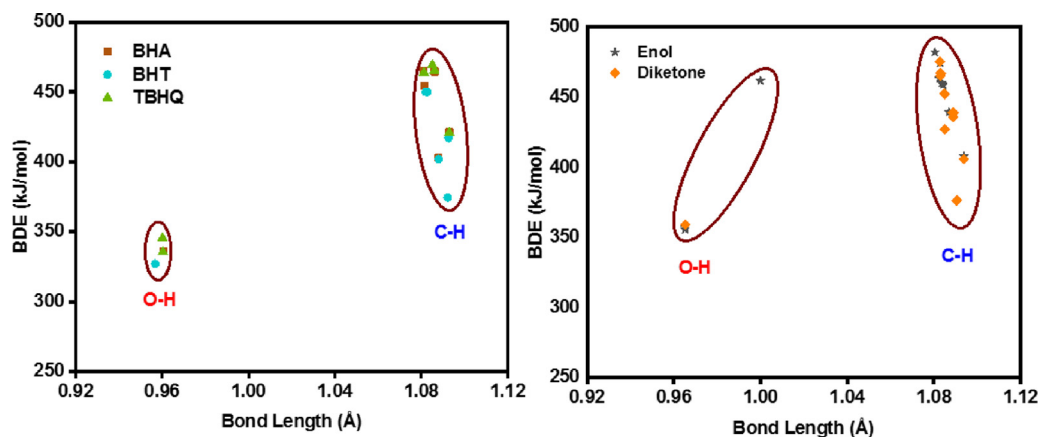
Fig. 6. Bond dissociation enthalpies (BDEs) vs bond length in case of butylated hydroxytoluene - BHT, butylated hydroxyanisole - BHA, *tert*–butylhydroquinone – TBHQ (left panel), and curcumin A and D (right panel) antioxidant additives. All compounds have been computed at the M06–2X/6–311+*G*(d,p) level of theory in gas phase.

Table 4

Ionization potential (IP) and lowest proton dissociation enthalpy (PDE) values (in kJ/mol) of butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA), *tert*–butylhydroquinone (TBHQ), curcumin A, and D calculated at the M06–2X/6–311+*G*(d,p) level of theory in gas phase.

Compound	IP	PDE	IP+PDE
BHA	726.0		
O–H		920.9	1646.9
C7–H		988.0	1714.0
BHT	728.9		
O–H		909.0	1637.9
C7–H		956.5	1685.4
TBHQ	741.3		
O1-H		905.1	1646.4
O2-H		915.1	1656.4
C7-H		990.5	1731.8
Curcumin A	699.2		
O1-H		967.5	1666.7
O2-H		969.2	1668.4
O3-H		1033.7	1732.9
C21-H		1019.6	1718.8
Curcumin D	738.4		
O1-H		931.6	1670.0
O2-H		931.6	1670.0
C11-H		948.9	1687.3

Table 5

Lowest proton affinities (PA) and electron transfer enthalpy (ETE) values in kJ/mol for butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA), *tert*–butylhydroquinone (TBHQ), and curcumin A, and D calculated at the M06–2X/6–311+*G*(d,p) level of theory in gas phase.

Compound	PA	ETE	PA+ETE
BHA			
O–H	1447.5	199.3	1646.8
C7–H	1676.7	37.3	1714.0
BHT			
O–H	1417.3	220.7	1638.0
C7–H	1594.7	96.2	1690.9
TBHQ			
O1-H	1446.2	200.3	1646.5
O2-H	1458.8	197.7	1656.5
C7-H	1686.5	54.0	1740.5
Curcumin A (enol)			
O1-H	1380.7	286.0	1666.7
O2-H	1384.4	284.1	1668.5
O3-H	1436.8	296.2	1733.0
C21-H	1609.5	109.3	1718.8
Curcumin D (diketone)			
O1-H	1382.6	287.4	1670.0
O2-H	1383.1	287.0	1670.1
C11-H	1413.7	296.2	1709.9

The second studied antioxidant mechanism is the single electron transfer proton transfer (SETPT), which involves two steps, an electron transfer which is followed by a proton transfer (Fig. 3). To describe the process, the ionization potential (IP) of the antioxidants was calculated (first step – electron transfer to a free radical), which resulted in the formation of a radical cation, and then, the proton dissociation enthalpy (PDE) was calculated (second step – proton transfer from the radical cation). The value of IP relates to the energy necessary to remove an electron from the neutral antioxidant compound, whereas the PDE value shows the enthalpy of deprotonation of the antioxidant radical cation. The lower the IP and PDE values, the greater the antioxidant potential of the molecule [53]. The computed ionization potentials (Table 4) indicate that curcumin A requires the lowest energy (699.2 kJ/mol) to donate an electron, so it has the highest potential to participate in such reaction among all additives followed by BHA, BHT, curcumin D, and TBHQ.

The computed PDE values show that the O–H bonds are preferred over the C–H bonds for deprotonation in all additives, which means that proton donation is preferable from an O–H of the antioxidant radical cation than from a C–H. The PDE values of O–H bonds for the compounds range from 905.1 to 1033.7 kJ/mol.

The lowest value is 905.1 kJ/mol for TBHQ and the highest is 1033.7 kJ/mol for curcumin A and located at the center of structure (O3-H). The molecules can be ranked based on their PDEs of O–H bonds as follows: curcumin *A* > curcumin *D* > BHA> BHT> TBHQ.

The third studied mechanism is the sequential proton loss electron transfer (SPLET), which also includes two steps (Fig. 3). First, a proton from the antioxidant molecules transferred and thus, an anion is formed, then, the electron transfer occurs from the antioxidant anion to the free radical. The antioxidant potential of the species in this mechanism has been characterized by computing the proton affinities (PAs) and the electron transfer enthalpy (ETE) values (Table 5).

The PA values for the natural compounds are smaller than for the synthetic antioxidant additives for each of the studied O–H and C–H bonds. The PA values of O–H bonds for the studied compounds range from 1380.7 to 1458.8 kJ/mol. The lowest value is 1380.7 kJ/mol belongs to curcumin A (O1-H) and the largest one is 1458.8 kJ/mol and the corresponding hydrogen can be found in TBHQ (O2-H). While for C–H bonds, the results indicated that, the lowest value is associated with C11-H (1413.7 kJ/mol) in curcumin D and the strongest one is C7-H (1686.5 kJ/mol) and located in

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